REMARKS/ARGUMENTS

Claims 1, 20, 24-25, 28-31 and 33-34 are pending and are currently under examination. Claim 1 was previously amended in the prior Amendment to recite: (1) "[a] method for treating HIV infection in a human infected with the HIV infection;" and (2) "wherein the stem cell-rich population of cells has ***been screened to identify that it has*** a beneficial gene that is a homozygous polymorphism in a CCR5 gene and the encoded CCR5 receptor does not facilitate HIV entry into the immune cell, ***wherein in the polymorphism is a 32 basepair deletion in the coding region of the CCR5 gene***, . . ." Reconsideration is respectfully requested.

In the Office Action, claims 1, 20, 24-25, 28-31 and 33-34 were rejected, in various combination, under 35 U.S.C. § 103. For the reasons set forth herein, each of these rejections is overcome.

I. REJECTIONS UNDER 35 U.S.C. § 103(A)

A claim is considered obvious "if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103(a). The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385, 1395-97 (2007) identified a number of rationales to support a conclusion of obviousness which are consistent with the proper "functional approach" to the determination of obviousness as laid down in *Graham*. The key to supporting any rejection under 35 U.S.C. § 103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. The Supreme Court in *KSR* noted that the analysis supporting a rejection under 35 U.S.C. § 103 should be made explicit. One of the rationales addressed by the court in *KSR* supports a finding of obviousness when the prior art reference (or combination of references): (1) teaches or suggests the claim elements; (2) provides some suggestion or motivation to combine the references; and (3) provides a reasonable expectation of success. M.P.E.P. § 2143.

A. Piccachio et al. in view of Contu et al. and Hariharan et al.

Claims 1, 20, 24-25, 30 and 31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Piccachio *et al.* (*J. Virol.*, 71(9):7124-7127 (1997); hereinafter "Piccachio *et al.*), Contu *et al.* (*Bone Marrow Transplant*, 12:669-671 (1993); hereinafter "Contu *et al.*") and Hariharan *et al.* (*AIDS Res. Hum. Retroviruses*, 15(17):1545-1552 (1999); hereinafter "Hariharan *et al.*"). For the reasons set forth herein, Applicants respectfully traverse this rejections.

Applicants assert that the combination of references cited by the Examiner simply fails to teach or suggest all of the elements of the presently claimed method.

Piccachio *et al.* disclose that "[i]ndividuals homozygous for a 32-bp deletion (Δ32) in the CCR5 gene encoding the correceptor for macrophage-tropic human immunodeficiency virus type 1 (HIV-1) ***are resistant to virus infection, and heterozygous individuals show some slowing of disease progression***" (*see*, Abstract of Piccachio *et al.*). Importantly, Piccachio *et al.* do **not** teach or suggest treating HIV infection in a human ***infected*** with the HIV infection, nor do Piccachio *et al.* teach or suggest the presently claimed method of treating HIV infection in a human infected with the HIV virus.

Contu *et al.* do **not** provide the teachings that are missing from Piccachio *et al.* In the Office Action, the Examiner states:

> The deficiency of Piccachio *et al.* is cured by Contu who reported the identification of HLA genotype of allogeneic bone marrow cells and reported administering HLA-identical allogeneic bone marrow cell transplant to a human subject infected with HIV after cytoablation with busulphan and cyclophosphamide. ***To the extent that Contu et al. describe transplanting HLA-identical bone marrow cell to a HIV infected human, the rejection is applicable to the instant case.*** Applicants' selective reading of Piccachio et al. ignores the teachings of Contu.

See, page 9 of the Office Action (emphasis added).

However, contrary to the Examiner's allegation, the teachings of Contu *et al.*, either alone in combination with Piccachio *et al.*, do **not** teach or suggest the presently claimed method of treating HIV infection. Instead, Contu *et al.* report on a 25 year-old woman with

AIDS that was submitted to HLA-identical allogenic ***bone marrow transplant*** (BMT) after cytoablation with busulphan and cyclophosphamide and combined anti-HIV-1 therapy with zidovudine, IFN-alpha 2 and anti-HIV-1-specific T cell clones. Contu *et al.* note that marrow engraftment occurred after 18 days, tests for HIV-1 were negative after 30 days, but the hematologic reconstitution of the patient was poor. Contu *et al.* further note that the eventual development of ARDS led to the death of the patient 10 months after transplantation.

The presently claimed method of treating HIV infection in a human infected with the HIV virus does **not** involve transplanting HLA-identical bone marrow cells to a HIV infected human. Instead, the presently claimed method of treating HIV infection in a human in need thereof involves transplanting into the human ***a stem cell-rich population of cells*** from a human donor, wherein ***the stem cell-rich population of cells has been screened to identify that it has a beneficial gene that has a homozygous polymorphism in a CCR5 gene*** and the encoded CCR5 receptor does not facilitate HIV entry into the immune cell, wherein the polymorphism is a 32 basepair deletion in the coding region of the CCR5 gene and ***wherein the stem cell-rich population of cells is umbilical cord blood.***.

As with Contu *et al.*, Hariharan *et al.* do **not** provide the teachings that are missing from Piccachio *et al.* In the Office Action, the Examiner states:

> ***Hariharan et al. disclose the advantage of using human placental cord blood (HPCB) as being a rich source of hematopoietic stem cells having considerably greater proliferative capabilities*** compared to similar cells from bone marrow (page 1546, column 1, lines 3-5), ***the rejection is applicable to the instant case***.

See, page 10 of the Office Action (emphasis added).

However, Applicants are **not** claiming human placental cord blood as a rich source of hematopoietic stem cells. In fact, the presently claimed method has nothing to do with human placental cord blood. Instead, claim 1, as previously amended, requires that "the stem cell-rich population of cells is ***umbilical cord blood***." Moreover, Applicants respectfully submit that the teachings of Hariharan *et al.*, which include the finding that "CCR5 protein, the major macrophage-tropic HIV-1 coreceptor, was **not** expressed in freshly isolated HPCB

$CD34^{+}AC133^{+}$ stem cells," come ***nowhere close*** to teaching the presently claimed method. The Examiner notes that "Hariharan cite Ruiz et al who reported cultured CD34+ showed surface expression of CCR5 receptor (see page 1551, col. 1, para 1)" (*see*, page 10 of the Office Action). However, the Ruiz *et al.* reference is not of record in the present case, and even if it does demonstrate surface expression of CCR5 receptors, this finding is not tantamount to teaching the presently claimed method of treating HIV infection in a human infected with the HIV cirus.

Clearly, whether the cited references are looked at individually or in combination with each other, Piccachio *et al.*, Contu *et al.* and Hariharan *et al.* do **not** teach or suggest the presently claimed method of treating HIV infection in a human in need thereof by transplanting into the human a stem cell-rich population of cells from a human donor, wherein ***the stem cell-rich population of cells has been screened to identify that it has a beneficial gene that has a homozygous polymorphism in a CCR5 gene*** and the encoded CCR5 receptor does not facilitate HIV entry into the immune cell, wherein the polymorphism is a 32 basepair deletion in the coding region of the CCR5 gene and ***wherein the stem cell-rich population of cells is umbilical cord blood.***.

In view of the foregoing, Applicants submit that the references cited by the Examiner cannot be used to support a legal conclusion of obviousness because there is simply no rational underpinning to combine them to arrive at the present invention. Therefore, Applicants respectfully request that the Examiner withdraw the present rejection under 35 U.S.C. § 103(a).

B. Piccachio et al., Contu et al. and Hariharan et al., as applied to claims 1, 24, 28-31 and 33-34, and further in view of Kaneshige et al.

Claims 1, 20, 24-25, 30 and 31 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Piccachio *et al.*, Contu *et al.* and Hariharan *et al.*, as applied to claims 1 and 24, above, and further in view of Kaneshige *et al.* (*MHC &IRS*, (1):159-164 (1994); hereinafter "Kaneshige *et al*"). For the reasons set forth herein, Applicants respectfully traverse this rejections.

For the reasons set forth above, Piccachio *et al.*, Contu *et al.* and Hariharan *et al.* do not teach or suggest the presently claimed method of treating HIV infection. Moreover,

Kaneshige *et al.* do not provide the teachings that are missing from Piccachio *et al.*, Contu *et al.* and Hariharan *et al.*. Kaneshige *et al.* teach methods for HLA class II genotyping by a reverse dot blot method. Kaneshige *et al.* provide **no** teachings regarding HIV infection in humans or methods for treating HIV infection in humans.

Accordingly, Applicants respectfully request that the Examiner withdraw the present rejection under 35 U.S.C. § 103(a).

C. Rader et al., Balotta et al. and Hariharan et al.

Claims 1 and 24-25 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rader *et al.* (US Publication No. 2003/0039642; hereinafter "Rader *et al.*"), Balotta *et al.* (*AIDS*, 11(10):F67-71 (1997); hereinafter "Balotta *et al.*") and Hariharan *et al.* For the reasons set forth herein, Applicants respectfully traverse this rejections.

As pointed out by the Examiner, Rader *et al.* disclose a method for treating a patient infected with HIV, the method comprising the steps of: administering **CCR5-def hematopoietic stem cells** to the patient via intravenous injection; **and** administering **CCR5-def neuronal stem cells** to the patient via subcutaneous injection. However, this method is fundamentally different from the presently claimed method. In fact, as pointed out by the Examiner, Rader *et al.* ***differ*** "from the claimed invention by **not** disclosing screening polymorphism of CCR5 gene being 32 bp deletion in the coding region of the CCR5 gene" (*see*, page 12 of the Office Action (emphasis added)).

Balotta *et al.* do **not** cure the deficiencies of Rader *et al.* Balotta *et al.* analyzed the polymorphism of CCR5 gene in HIV-1 infected and uninfected individuals. In doing so, Balotta *et al.* do not teach or suggest the presently claimed method. In fact, as pointed out by the Examiner, "Balotta *et al.* do **not** teach screening polymorphism of CCR5 gene in stem cell population derived from cord blood" (*see*, page 12 of the Office Action (emphasis added)), nor do Balotta *et al.* teach or suggest a method of treating HIV infection.

Further, the teachings of Hariharan *et al.*, which, as noted above, include the finding that "CCR5 protein, the major macrophage-tropic HIV-1 coreceptor, was **not** expressed

in freshly isolated HPCB $CD34^{+}AC133^{+}$ stem cells," come ***nowhere close*** to teaching the presently claimed method.

As such, Rader *et al.*, Balotta *et al.* and Hariharan *et al.*, either alone or in combination, do **not** teach or suggest the presently claimed method of treating HIV infection in a human in need thereof by transplanting into the human a stem cell-rich population of cells from a human donor, wherein ***the stem cell-rich population of cells*** has been screened to identify that it ***has a beneficial gene that has a homozygous polymorphism in a CCR5 gene*** and the encoded CCR5 receptor does not facilitate HIV entry into the immune cell, ***wherein the polymorphism is a 32 basepair deletion in the coding region of the CCR5 gene***.

In view of the foregoing, Applicants submit that the references cited by the Examiner cannot be used to support a legal conclusion of obviousness because there is simply no rational underpinning to combine them to arrive at the present invention. Therefore, Applicants respectfully request that the Examiner withdraw the present rejection under 35 U.S.C. § 103(a).

D. Rader et al., Balotta et al. and Hariharan et al., as applied to claims 1 and 24-25, and further in view of Kaneshige et al.or Contu et al.

Claims 1 20, 28-31 and 33-34 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Rader *et al.*, Balotta *et al.* and Hariharan *et al.*, as applied to claims 1 and 24-25, above, and further in view of Kaneshige *et al.* or Contu *et al.* For the reasons set forth herein, Applicants respectfully traverse this rejections.

As explained above, Rader *et al.* disclose a method for treating a patient infected with HIV, the method comprising the steps of: administering **CCR5-def hematopoietic stem cells** to the patient via intravenous injection; **and** administering **CCR5-def neuronal stem cells** to the patient via subcutaneous injection. This method is fundamentally different from the presently claimed method. Again, as pointed out by the Examiner, Rader *et al.* ***differ*** "from the claimed invention by **not** disclosing screening polymorphism of CCR5 gene being 32 bp deletion in the coding region of the CCR5 gene" (*see*, page 12 of the Office Action (emphasis added)).

Moreover, as discussed above, Balotta *et al.*, Hariharan *et al.*, Kaneshige *et al.* and Contu *et al.* do **not** supply the teachings missing from Rader *et al.*. It is clear that the cited

references, either alone or in combination, do **not** teach the presently claimed method the presently claimed method of treating HIV infection in a human in need thereof by transplanting into the human a stem cell-rich population of cells from a human donor, wherein ***the stem cell-rich population of cells*** has been screened to identify that it ***has a beneficial gene that has a homozygous polymorphism in a CCR5 gene*** and the encoded CCR5 receptor does not facilitate HIV entry into the immune cell, ***wherein the polymorphism is a 32 basepair deletion in the coding region of the CCR5 gene*** and ***wherein the stem cell-rich population of cells is umbilical cord blood.***.

Absent such a teach or suggestion, the presently claimed method is non-obvious and, thus, patentable. Therefore, Applicants respectfully request that the Examiner withdraw the present rejection under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Further, the Commissioner is hereby authorized to charge any additional fees or credit any overpayment in connection with this paper to Deposit Account No. 20-1430.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,

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